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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,674	08/26/2006	Julia Adam-Worrall	2004.831US	2842

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EXAMINER	
LOEWE, SUN JAE Y	
ART UNIT	**PAPER NUMBER**
1626	

MAIL DATE	DELIVERY MODE
01/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,674	ADAM-WORRALL ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8 and 10-15* is/are pending in the application.

4a) Of the above claim(s) *10,11,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8 and 12* is/are rejected.

7)☒ Claim(s) *6 and 13* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

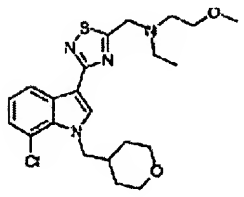
1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-12-2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-6, 8 and 10-15 are pending in the instant application. Claims 7 and 9 were cancelled by preliminary amendment filed on August 26, 2006.

Election/Restrictions

2. Applicant's election with traverse of Group II, and species of " 7-chloro-3-(5-{[N-ethyl-N-(2-methoxyethyl)amino]methyl}-[1,2,4]-thiadiazol-3-yl)-1-(tetrahydropyran-4-yl)methyl-1H- indole" (see structure below), in the reply filed on November 28, 2007 is acknowledged.



The traversal is on the ground(s):

a) " separation of the invention into Group I, R1=cyclohexyl and Group II, R1=tetradynopyranyl appears to violate the rule of one general inventive concept."

See MPEP 1893.03(d):

> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature.

For the reasons provided in the restriction requirement dated November 2, 2007 the species of Formula I do not related to a single general inventive concept (see page 4).

b) " It is also respectfully submitted that the Examiner would not suffer an undue burden of searching "

The instant application is a national stage entry of PCT/EP05/50833 and thus the criteria of burden (MPEP 800, for national applications filed under 35 USC 111) does not apply.

The arguments are not found persuasive for the reasons discussed above. The restriction requirement is still deemed proper and is therefore made FINAL.

3. The following guidelines are provided by MPEP 1893.03(d):

> " Note: the determination regarding unity of invention is made without regard to whether a group of inventions is claimed in separate claims or as alternatives within a single claim. The basic criteria for unity of invention are the same, regardless of the manner in which applicant chooses to draft a claim or claims.
>
> >If an examiner (1) determines that the claims lack unity of invention and (2) requires election of a single invention, when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder. Any nonelected product claim that requires all the limitations of an allowable product claim, and any non-
>
> ¶ *18.20 National Stage Election of Species in 35 U.S.C. 371 Applications*
>
> Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If "

The generic claims were not allowable (Sections 8-13). Pursuant MPEP 1893.03(d), non-elected species were withdrawn from further consideration.

4. Claims 10, 11, 14 and 15 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter. Applicant timely traversed the restriction (election) requirement in the reply filed on November 28, 2007.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on March 12, 2007 was in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The IDS was considered. A signed copy of form 1449 is enclosed herewith.

Claim Objections

7. Claims 1-5, 6, 8, 12 and 13 objected to for containing non-elected subject matter.

8. Claim 6 objected to because of the following informality: the claim is not written in proper Markush format (MPEP 803.02). The following correction is suggested: insert the term "and" between - 7-Chloro-3-(4-{[*N*-(2-methoxyethyl)-*N*-methylamino]methyl}-[1,3]-thiazol-2-yl)-1-(tetrahydropyran-4-yl)methyl-1*H*-indole; and

- 7-Chloro-3-{5-[(2,2-dimethyl-pyrolidin-1-yl)methyl]-[1,2,4]oxadiazol-3-yl}-1-(tetrahydropyran-4-yl)methyl-1*H*-indole;

9. Claim 1 objected to because of the following informality. The following two entries appear to be duplicates:

"R, when present in X_2 or X_3, may form together with R_3 a 5-8 membered ring;" and

"R_3 together with R, when present in X_2 or X_3, forms a 5-8 membered ring;."

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-5, 8 and 12 rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

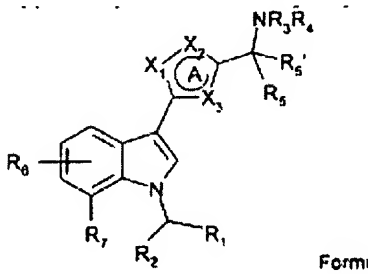
> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (ie. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph). Below is such comparison.

I. ***Scope of Claims (based on a subgenus of compounds within elected Group II)***

Compounds of Formula I with the following structural limitations: R^1=tetrahydropyran, Ring A=(1,2,4)-thiadiazole, R_2 and R_7 do not form ring.



Formula I

All variables are claimed *broader* than what is supported by the disclosure (see below section II):

R^3:	for all claims *except* claim 3
R^4:	for all claims
$R^5/R^{5'}$:	for all claims
R^6:	for all claims

II. Scope of Disclosure

Reduction to Practice:

The compounds reduced to practice support the following definitions for the variables

R^3:	H, (C_{1-6})alkyl
R^4:	H, (C_{1-6})alkyl or
R^3 and R^4 form pyrrolidine or morpholine	
$R^5/R^{5'}$:	H or (C_{1-4})alkyl;
R^6:	H, (C_{1-4})alkyl.

Reduction to Structural or Chemical Formulas:

There is no disclosure of species (eg. by reduction to structural/chemical formulas) in addition to those reduced to practice.

Correlation between Structure and Function:

Structure-activity studies (SAR) are disclosed in the art for the cannabinoid receptor (eg CB1) agonists/antagonists for genuses of compounds different from those instantly claimed. Although these studies do not address the activity of the compounds of the instant genus as a function of structural modifications, they do show that a compound's ability to bind and modulate this receptor is influenced by structural changes to the common chemical core (eg. see below section 11). Because instant specification does not disclose a correlation between function and structure, and because such correlation is not commonly known in the art, one of ordinary skill would not know what *specific*

structural elements would allow for preservation of activity within the unrepresented genus.

III. *Analysis of Fulfillment of Written Description Requirement:*

In the absence of a correlation between structure and function, it is not possible to know what modifications to the instantly claimed core structure will allow for the preservation of the desired activity.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by claims 1-5, 8 and 12; (ii) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus/subgenus claimed; (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

(Enablement)

11. Claims 1-5, 8 and 12 rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for making and using compounds that have adequate written description. The specification is not enabling for using compounds that are not supported by the disclosure, as the only utility disclosed is that towards the CB1 receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

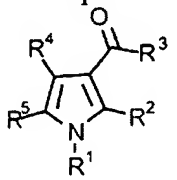
The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims
Claims drawn to compounds that *do not* have written description support.

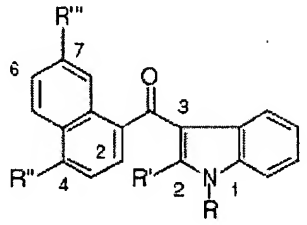
The nature of the invention
The compounds are disclosed to be agonists of the CB1 receptor. Additional utility is neither disclosed nor known in the art.

The state of the prior art/level of ordinary skill/level of predictability
The level of ordinary skill is high, but the level of predictability in the art is low. The binding ability and activity of a compound towards a receptor depends on the interaction between the chemical groups/moieties of the compound with specific residues in the binding pocket of the protein/receptor. It is well documented in the art that changes to the structure/chemical properties of a compound can have unpredictable results on its overall binding and/or functional binding ability. Studies suggest that this is the case with the CB1 receptor, note illustrative example below:

- Tarzia et al (p. 3969, Table 1): SAR studies of CB1 receptor agonists of the structure below disclosed that varying the R1 substituent, for example, may lead to compounds within the genus that are inactive towards the receptor.



- Huffman et al. (p. 91, Table 1): SAR studies of CB2 receptor agonists of the structure below disclosed that varying R substituent from pentyl to propyl changes the Ki (nM) for binding to the CB1 receptor from 9 ± 5 to 1050 ± 55.



Note: examples above provided to illustrate inability to predict activity and/or binding of a compound towards CB1 receptor as a function of changing the nature of the variables to the core structure.

As discussed in section 10, it is not known what specific structural changes are tolerated for producing active CB1 receptor modulators. One of ordinary skill could not predict which of the structurally diverse compounds, embraced by the claims but not exemplified/supported by the disclosure, would possess the desired activity. Lacking use as CB1 agonists, in view of the absence of an alternate utility, one of ordinary skill is not enabled by the disclosure to use the compounds which do not have written description support.

The amount of direction provided by the inventor/existence of working examples
Direction and working examples limited to the compounds that are adequately represented by the disclosure (Section 10.II)

The quantity of experimentation needed to make or use the invention
It would require undue experimentation for one of ordinary skill to first test which of the compounds possess this activity before being able to practice the invention commensurate in scope with the breadth of the instant claims.

Claim Rejections – 35 USC 112 2nd Paragraph

12. Claim 1 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is drawn to "(indol-3-yl)-heterocycle derivative having the general Formula I." The term "derivative" is defined as organic compounds obtained from another compound by a simple chemical process or an organic compound containing a structural radical similar to that from

which it is derived (Hackh's chemical dictionary, 1972). Furthermore, the term "general" makes it unclear whether Applicant is claiming only compounds encompassed by the Markush formula I, or compounds that are structurally similar to those defined by Markush formula I. Therefore, the terms "derivative" and "general" render the claims indefinite because the metes and bounds cannot be ascertained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

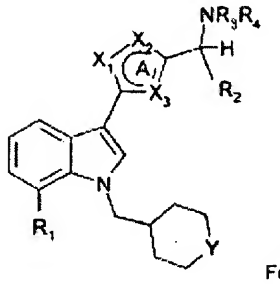
with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-5, 8 and 12 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 8 and 9 of copending Application No. 11/506,579. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons below.

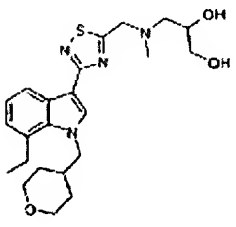
This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Determination of the scope and contents of claim 1-5, 8 and 9 of US Appl. 11/506,579.
The claims are drawn to a Markush group of compounds with the same utility as that instantly claimed.



Formula I

Preferred embodiments disclosed include, for example, the species:



7-Ethyl-3-[(5-{[*N*-(2,3-dihydroxypropyl)]-methylamino}methyl)-([1,2,4]-thiadiazol-3-yl)]-1-(tetrahydropyran-4-yl)methyl-1*H*-indole,

Ascertaining the differences between claims 1-5, 8 and 9 of US Appl. 11/506,579 and the claims at issue.
The preferred embodiment (above) anticipates the instant claims.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.
MPEP § 2144.08.II.A.4(c) states "...consider teachings of a preferred species within the genus. If such a species is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties". This is a "Genus-Species Guidelines" for the examination based on 35 U.S.C. 103. An analogous guideline was followed here for the analysis of obviousness-type double patenting.

The preferred embodiment suggests to one of ordinary skill to practice the instant invention of claims 1-5, 8 and 12. Thus, the instant claims are *prima facie* obvious over claims 1-5, 8 and 9 of US Appl. 11/506,579.

Conclusion

14. No claims allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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